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Experimental Studies on Thoracic Inferior Vena Cava Constriction in Dogs, with Special Reference to the Alteration on Their Hepatic Clearance

by

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I. INTRODUCTION

In a previous paper,[16] we reported 6 cases of membranous obstruction of the inferior vena cava at the hepatic portion, of which 4 cases were successfully treated by transcardiac membranotomy.

Autopsy of the unfortunate cases of ours and other authors[10)14)15)24)26)29)32)35] revealed that the most impressive pathologic changes were observed in the liver besides the inferior vena cava itself.

The marked liver congestion, congestive cirrhosis of the liver observed at autopsy seemed to demonstrate that hemodynamic changes in hepatic blood flow were highly responsible for the fatality of this disease. Since MC KEE[19] produced experimental ascites by constricting the inferior vena cava, many experimental studies[3)4)11)25] have been made regarding the alterations provoked in a living body by the suprahepatic caval constriction.

However, they observed the alterations principally in acute conditions or in relatively short postoperative period, while in clinical cases, especially in those to whom surgical treatments were indicated, it is clear that the changes observed there had developed or persisted for years in patients.

Hence, it seems to be of significance to follow up the alterations in hepatic functions over a long period of time throughout the course of the disease. For the pourpose, gradual constriction of the thoracic inferior vena cava was produced in the present experiments using dogs in order to survive them over a long period of time after the operation. To estimate hepatic blood flow, radioactive ^{198}Au colloid clearance and BSP clearance were selected as indicators to follow up their alteration among various hepatic function tests, because these indicators seemed to correspond the changes which may presumably be provoked in the dogs after the operation. Parallel observations were also carried out in the development of collateral circulations and histological changes in the abdominal organs.

II. EXPERIMENTALS

1) The experimental production of gradual constriction in the thoracic inferior vena cava of dogs.

Since PAGE[27] discovered the fibroblastic action of a polythene-type of cellophane, which thenceforth was found to be exerted by dicetyl phosphate, the cellophane or dicetyl phosphate has been utilized in projects of the gradual narrowing of the various luminal

organs[1)27)] in anticipation of the cicatrical shrinkage.

Recently in this country, experimental coronary insufficiency was successfully produced by NAKAMURA[22)] utilizing dicetyl phosphate in a new way which is characterized by the use of gelatine sponge and aluminium plate. This method was employed for the purpose of gradual constriction of the inferior vena cava with some modification.

Procedure :

i) Preparation of the instrument used for the constricting.

Dicetyl phosphate crystal (0.5g) was dissolved in 12 cc of ethanol by heating, and the resulting solution was poured diffusely into 10 cc of gelatine sponge. (Spongel : manufactured by Yamanouchi Co. Japan) The sponge soaked with the solution was kept in a desicator for a week to evaporate ethanol.

Then the gelatine sponge containing recrystallized and homogeniously spred dicetyl phosphate was divided into small pieces (3mm×5mm×15mm in size), which were adhered on a thin aluminium plate (0.5mm in thickness, 20mm×40mm in area), as illustrated in figure 1.

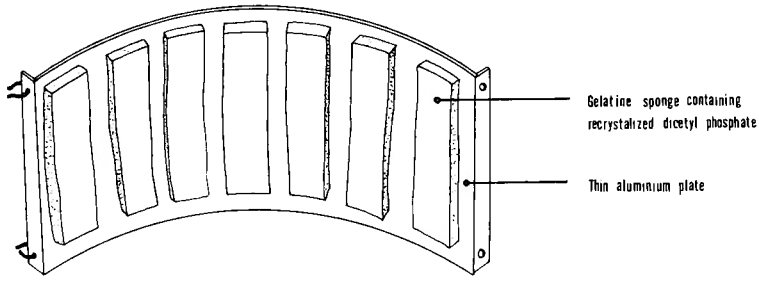

Fig. 1 The instrument used for the constriction

Every procedures above mentioned were done under aseptic condition.

ii) Operation

Mature healthy dogs ranging in weight from 6 to 14 kg were anesthetized with intravenous administration of 0.5 cc per kg of body weight of nembutal solution so that the wink reflex may scarcely remain.

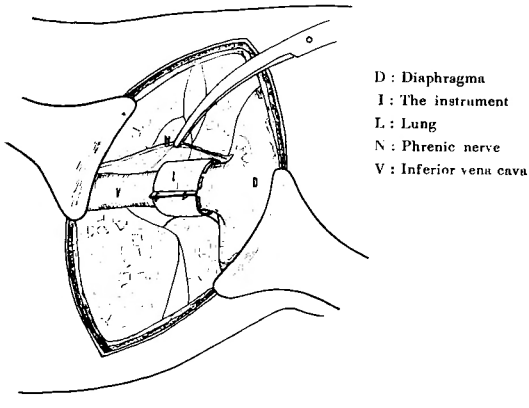

Fig. 2 Operation : right thoracotomy and attachment of the instrument to the thoracic inferior vena cava

During the following operation, the animals were intubated and their respiration was maintained by the controlled positive pressure breathing using pure O_2 through a close-type apparatus.

A right thoracotomy was performed in the seventh intercostal space. The thoracic inferior vena cava was isolated from the phrenic nerve and the surrounding tissues, and the length of the circumference of the vessel was measured with a thin polyethylene tube. The aluminium plate prepared

as above mentioned was cut into adjusting size to the length of the circumference, and rounded to form a cylinder.

Thereafter the isolated inferior vena cava was surrounded wholly by the rounded plate, of which both ends were closed surely by two small clips, as illusrated in figure 2, the constriction of the inferior vena cava was not performed in this procedure in order to avoid acute hemodynamic changes. The thorax cavity was closed routinely after the reinflation of the lung. Then 300,000 units of penicillin was injected intramuscularily to prevent postoperative infection.

After the operation, the animals were fed with usual kennel diet and kept in the animal cages.

2) Measurement of ^{198}Au colloid clearance and BSP clearance

i) Procedure

Two milliliters of ^{198}Au colloid (supplied from the radiochemical center. Harwell, Amersham, England.) having about 50μC of radioactivity per 1 cc was intravenously given to the dogs previously anaesthetized with intravenous administration of nembutal.

Thereafter carefully timed 1 cc of blood samples were withdrawn with heparinized syringe from the femoral artery of dogs ten times with the interval of one minute. Then 1 cc of each blood sample exactly measured with pipette was transferred to a small test tube. The radioactivity in each samples was measured with Well-type sintiration counter.

Soon after these prosedures, 5 mg of bromsulfalein per kg of body weight was intravenously given to the dogs. Thereafter 3 cc of carefully timed blood samples were obtained from the femoral artery four times at 3, 6, 9, and 12 minutes after the injection. Each blood sample was transferred to a test tube using due care to avoid hemolysis. These blood samples were centrifuged for. 10 minutes at 2,000 revolutions per minutes.

The concentration of bromsulfalein in resulting serum was measured by GAEBLER's method[6] using BECKMANN spectrophotometer as described below. 0.5 cc of serum sample was placed in clean dry tube and added 2.5 cc of water and 3.0 cc of 0.1 N sodium hydroxide. The resulting solution was poured and filled 3 cc cell with 1 cm light path. The bromsulfalein dye concentration was calculated from the optical dencity of the solution against a water blank at 620 and 580 mμ filter. The results in mg of bromsulfalein per 10 cc of serum were given by the following formula.

$$\frac{E\ 580 - 1.2\ E\ 620}{0.0655}$$

ii) Calculations of ^{198}Au colloid clearance and BSP clearance

The logarithm of the radioactivity in countes or of the plasma dye concentration in mg per 10 cc is plotted against time in minutes. The intercept of the extrapolated line with the ordinate, when time equals zero (To), provides an estimate of the initial radioactivity or the dye concentration (Co). Thereafter T1/2, the time in minute corresponding to half deminished radioactivity or concentration 1/2Co, is obtained on the graph as illustrated in figure 3.

Then clearance coefficient K can be calculated by following theory and formula. Rapidness in deminishing of the concentration of a substance in circulating blood is proportional to the concentration, then

$$\frac{dC}{dt} = -KC$$

$$\log Ct = -Kt + \log Co$$

$$Ct = Coe^{-Kt}$$

$$-KT1/2 = -\log 2 \quad (\text{when } Ct = 1/2Co)$$

$$K = \frac{0.639}{T1/2}$$

Figure 3 and figure 4 illustrate sample calculations from the data obtained in the case of dog No. 12.

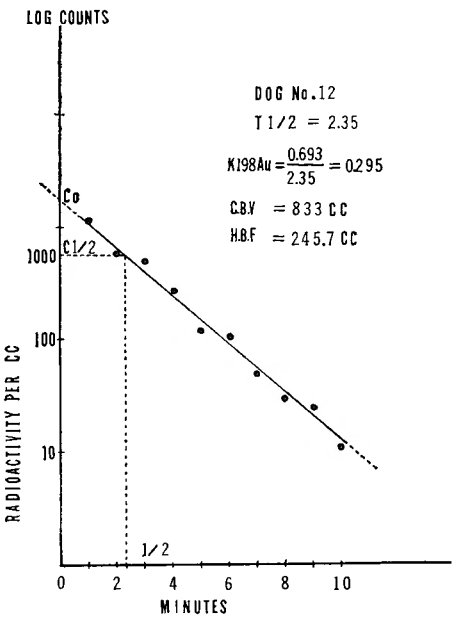

Fig. 3 A calculation of estimated hepatic blood flow in dog No. 12

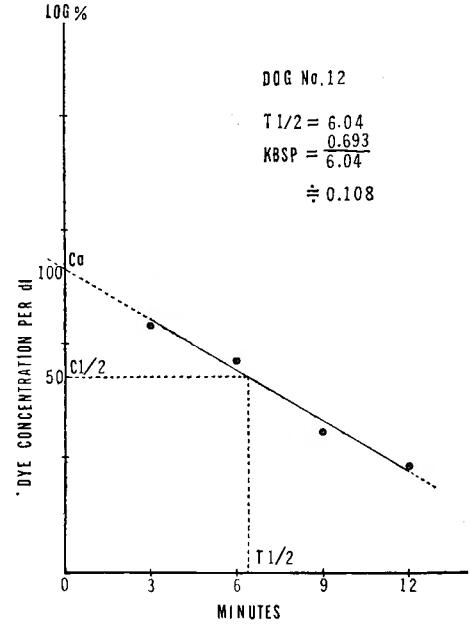

Fig. 4 A calculation of the coefficient of BSP clearance in dog No. 12

3. Measurement of circulating blood volume

Prior to the dye injection, 10 cc of blood sample was withdrawn from the femoral vein of the anaesthetized dog in order to obtain contrast serum.

0.1 cc of T-1824 solution per kg of body weight was then intravenously injected as rapid as possible. The injection requires about 30 seconds, and mean injection time is recorded as zero time.

Ten minutes after the injection, 10 cc of blood sample was withdrawn from the femoral artery. These two blood samples were centrifuged, and using the resulting serums, circulating plasma volume of the dog was determined by means of routine GREGERSON's method[8]. Haematclit value was determined by usual WINTROBE tube technique from the blood sample obtained at the midpoint of measurement of circulating plasma volume. The results in cubic centimeters of circulating blood volume were given by the following formula.

$$\frac{\text{circulating plasma volume} \times 100}{100 - \text{Haematclit } (\%)}$$

4. Roentogenological examination

State of the constriction of the thoracic inferior vena cava and development of the collateral circulations were observed by venograms.

Catheters of 1.0 mm in caliber were inserted into the femoral veins or, if possible, the saphenous veins of the anaesthetized dogs. the tips of the catheters were constantly kept in the external iliacal vein. Then 10 cc of 76 per cent urographine solution was injected as rapid as possible through the catheter, and simultaneously X-ray picture was taken. These procedures were repeated twice in a same dog in order to obtain the venograms of dorsoventral and lateral view.

5. Histpathological examination

The dogs were sacrificed at a period of six months, one year, one year and six months, or two years after the operation. Immediately after the gross observations of the organs in the thorax and the abdominal cavity, the liver; inferior vena cava, spleen, and kidney were removed and fixed in 10 per cent formaline solution.

Microscopic observation was carried out on these materials, with a special regard on the pathological changes in the liver, which were routinely prepared and dyed with hematoxylin eosin.

III. RESULTS

Out of 38 dogs subjected to this experiment, 10 dogs died within a week after the operation due to the outbreak of pneumothorax or intrathoracal infection. Of the other 28 dogs, 13 died within three months, 9 by too rapid constriction of the inferior vena cava, and 4 by various complications such as distemper, pneumonia and filariasis.

The rest 15 dogs survived for more than six months whose thoracic inferior vena cava had been constricted more than 1/2 of preoperative value in diameter. Of these 15 dogs, containing 2 totally obstructed, 6 survived more than one year. Ascites accumlation and marked development of the superfacial collateral circulations were observed in 24 cases. Photo. 1 illustrates the characteristic direction of blood flow flowing from below to upward.

1) ^{198}Au colloid clearance coefficient, BSP clearance coefficient, circulating blood volume, clearance ratio, and estimated hepatic blood flow in normal dogs.

Prior to the operation, the clearance coefficients and circulating blood volume were measured in dogs subjected to the present experiments as controls. The results are given in Table 1.

The mean reveals nearly midvalue of the other author's. Estimated hepatic blood flow and clearance ratio are able to calculate using these results. The results are given in Table 2.

2) Alteration in ^{198}Au colliid clearance coefficient and estimated hepatic blood flow after the operation.

Alterations in K ^{198}Au were followed up throughout the course. The measurement was carried out repeatedly with the interval of about three months.

Reduction of K ^{198}Au generally started at shortly after the period when ascites ac-

Table 2 Estimated Hepatic Blood Flow and Clearance Ratio in Normal Dogs.

Dog Number	Sex	Body Weight (kg)	E. H. B. F. (cc/min)	E.H.B.F. per Kg of Body Weight (cc/min/kg)	Clearance Ratio KBSP/K ^{198}Au
No. 1	♂	7.0	323.5	46.21	0.527
No. 6	♂	8.0	284.5	35.60	0.477
No. 7	♂	11.5	346.3	30.11	0.868
No. 9	♀	8.0	253.5	31.69	1.039
No. 10	♂	9.8	200.5	29.64	0.963
No. 11	♀	9.0	289.4	32.19	0.758
No. 12	♂	9.0	245.7	27.30	0.372
No. 13	♀	8.0	277.0	34.37	0.431
No. 14	♀	13.5	397.4	29.43	0.524
No. 15	♂	15.5	542.6	47.19	0.529
No. 16	♂	11.0	588.2	53.47	0.625
No. 18	♀	9.5	268.5	28.24	0.840
No. 20	♀	9.8	388.9	39.68	0.607
No. 21	♂	8.0	259.2	32.40	0.431
No. 22	♂	8.3	406.3	38.94	0.374
No. 23	♂	8.5	478.5	56.28	0.383
	Mean ± 2σ			39.12 ± 8.76	0.609 ± 0.210

Table 1 Circulating Blood Volume, ^{198}Au Clearance, and BSP Clearance in Normal Dogs.

Dog Numer	Sex	Body Weight	C. B. V. (cc/min)	KBSP (min^{-1})	K ^{198}Au (min^{-1})
No. 1	♂	7.0	793	0.210	0.408
No. 6	♂	8.0	823	0.165	0.346
No. 7	♂	11.5	1302	0.231	0.266
No. 9	♀	8.0	915	0.288	0.277
No. 10	♂	9.8	1088	0.257	0.267
No. 11	♀	9.0	1017	0.210	0.277
No. 12	♂	9.0	833	0.110	0.295
No. 13	♀	8.0	955	0.125	0.290
No. 14	♀	13.5	1577	0.132	0.252
No. 15	♂	15.5	1878	0.153	0.289
No. 16	♂	11.0	1910	0.193	0.308
No. 18	♀	9.5	1072	0.210	0.250
No. 20	♀	9.8	1124	0.120	0.346
No. 21	♂	8.0	1018	0.125	0.290
No. 22	♂	8.3	841	0.180	0.495
No. 23	♂	8.5	905	0.204	0.533
	Mean ± 2σ			0.189 ± 0.049	0.324 ± 0.084

C. B. V. : Circulating Blood Volume
KBSP : Clearance coefficient of BSP
K ^{198}Au : Clearance coefficient of 198Au

cumlation was first demonstrated. But after this initial reduction, K ^{198}Au remained in almost constant but in lowered level for a long period of time, without lining a chronic down -hill curve, while, circulating blood volume remained nearly constant or slightly increased especially in early stages of the constriction, hence in estimated hepatic blood flow, degree of its reduction was less than that of K ^{198}Au, as illustrated in Figure 5.

Conclusionally, it was revealed that the average value of estimated hepatic blood flow after its initial reduction decreased to 72 per cent of preoperative value, as illustrated in Figure 6.

3) Alteration in BSP clearance coefficient and clearance ratio after the operation.

Alterations in K BSP were followed up throughout the course. The measurement was carried out at the same period when K ^{198}Au was measured.

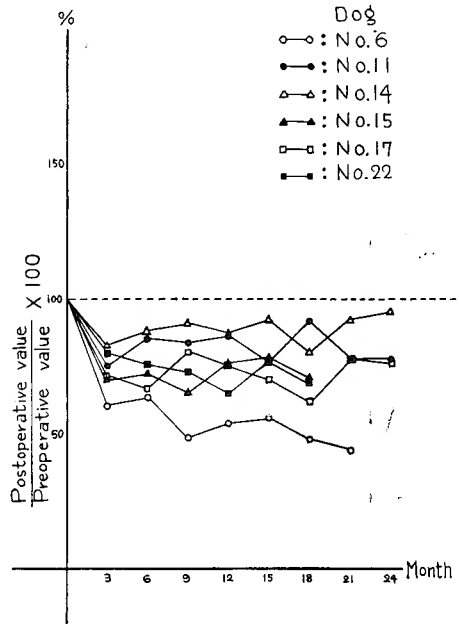

Fig. 5 Alteration in estimated hepatic blood flow after the operation

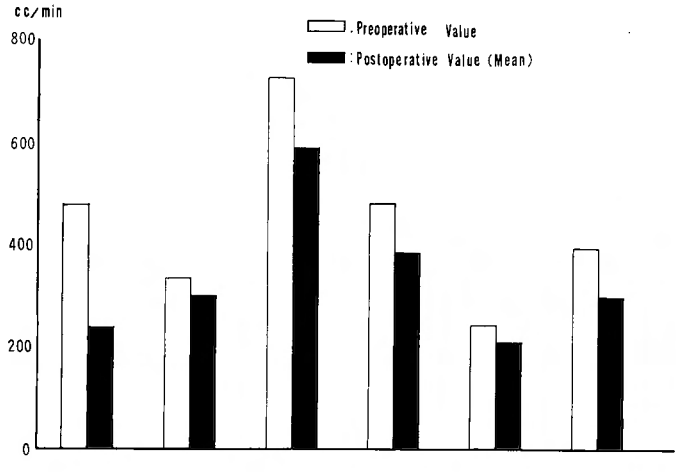

Fig. 6 Average postoperative value of estimated hepatic blood flow compared with preoperative value in 6 cases survived over more than one year

The results are given in Figure 7.

K BSP remained nearly normal over a long period of time after the operation. The initial reduction observed in K ^{198}Au was not demonstrated. But in the period when the shrinkage of the liver came to be observed macroscopically in a autopsy, the reduction of K was simultaneously observed.

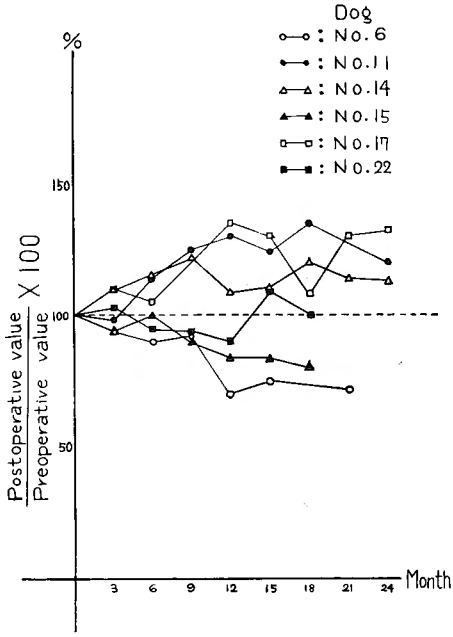

Fig. 7 Alteration in the coefficient of BSP clearance after the operation

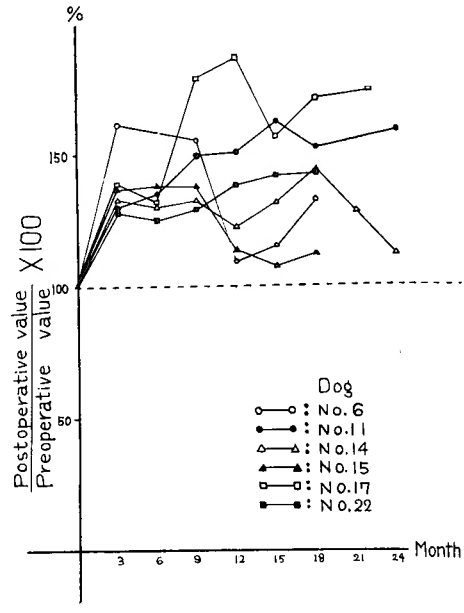

Fig. 8 Alteration in clearance ratio after the operation

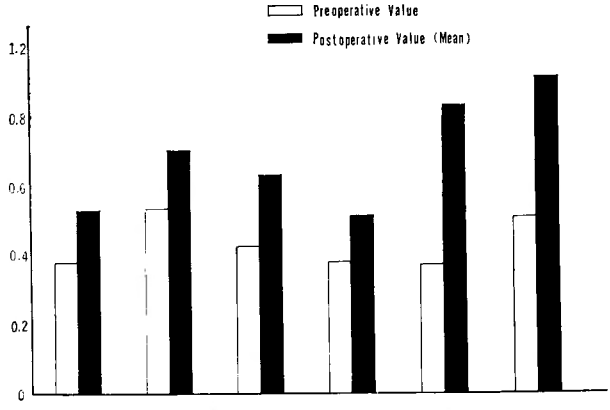

Fig. 9 Average postoperative value of clearance ratio compared with preoperative value in 6 cases survived over more than one year

Hereupon, alteration in clearance ratio was increased in initial stage of the constriction, and remained at a high level over a certain period of time till the final reduction occurred by subsequent cirrhosis of the liver. The rate of increasing in average value of clearance ratio was 40.1 per cent of its preoperative value, as illustrated in figure 8 and 9.

Figures 10, 11, 12, and 13 illustrate the alteration of these three indicators observed in four dogs.

4) Roentogenological findings

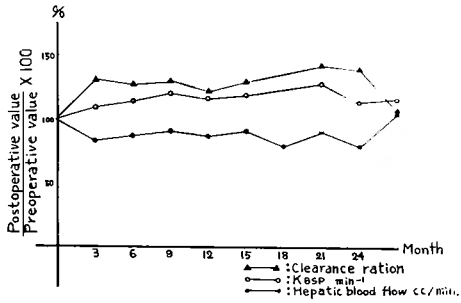

Fig. 10 Alteration of the three indicators of hepatic functions after the operation in dog No. 6

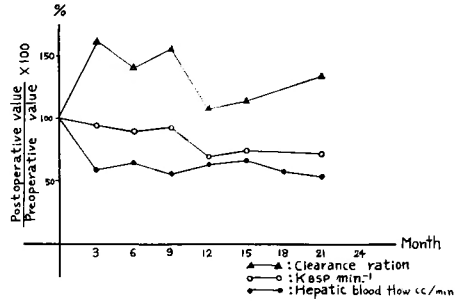

Fig. 11 Alteration of the three indicators of hepatic functions after the operation in dog No. 11.

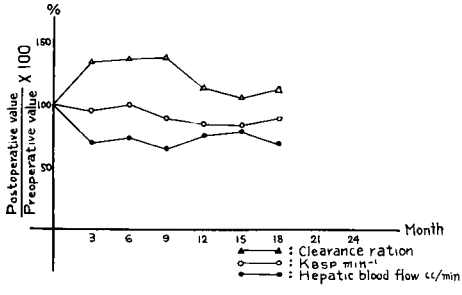

Fig. 12 Alteration in the three indicators of hepatic functions after the operation in dog No. 14

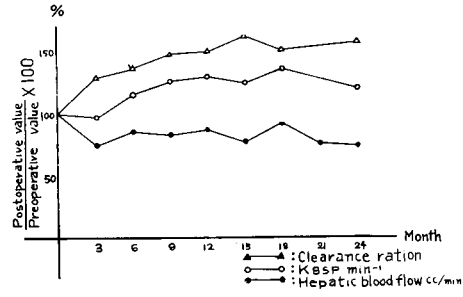

Fig. 13 Alteration in the three indicators of hepatic functions after the operation in dog No. 17

X-ray photographs in dorsoventral and lateral view were repeatedly taken with the interval of several months. Owing to the obstruction of the femoral veins and their branches subsequent to previously performed catheterization, it was unable to carry out this procedure at the exact intervals in some dogs. The constriction in the thoracic inferior vena cava was venographically observed generally at a period of three months after the operation, of which caliber ranging 1/4 to 1/2 of preoperative value. In 2 cases, perfect obstruction was observed. The development in collateral circulation was likewise observed in the venograms.

Two different types of the collateral circulation were observed there, as illustrated in photograph 5 and 6.

The first is deep, or paravertebral type, of which returning course of venous blood from the abdominal inferior vena cava to the superior vena cava was as follows. (Photo. 6)

Abdominal inferior vena cava ⟶ Vv. lumbales ⟶
Vv. lumbales ascendens ⟶ V. vertebralis ⟶
V. azygos ⟶ Vena cava superior

The second is superficial or parietal type, the returning course of which was as follows. (Photo. 5)

V. iliaca externa ⟶ V. epigastrica inferior ⟶

V. epigastrica superior ——→ V. mammalia interna ——→
V. subclavia ——→ Vena cava superior

these two types of collateral circulation were observed simultaneously when the thoracic inferior vena cava was constricted more than 1/2 of preoperative value in diamter, but venographically, the paravertebral type seemed to develop earlier than the other.

5) Autopsy and pathohistological findings

i) The inferior vena cava

The thoracic inferior vena cava was constricted or perfectly obstructed at the part surrounded with the aluminium cylinder by the granulation tissue which developed inside of the cylinder. Interstitial inflammations caused by foreign body were observed histologically in adventitia. Marked thickening of the venous wall was observed in the abdominal inferior vena cava. Histologically, hypertrophy was demonstrated mainly in the muscle layer of the wall, but partial thickening of the intima was also observed.

ii) The liver

In early periods of constricition, the enlarged dark reddish liver with sharp edge was constantly observed. Enlargement of the cental vein and its neighboring sinus filled with erythrocytes were histologically observed to a varying degree. In the period when the constriction was far advanced, the engorgement extended to the surrounding part of the lobulus, and atrophy and/or degeneration of the hepatic parenchymal cells, fibrosis in a central part of the lobulus were observed.

In some dogs which survived for longer periods, a characteristic macroscopic changes were observed in the liver. The extreme shrinkage of the liver with entirely rounded edges, and highly thickened liver capsule were so impressive that the liver resembled a sugar cake.

In these cases, exuberant fibrosis developed only in perilobar part of the liver while the centrilobar part remained nearly normal, and these two zones were obviously limited.

In the other dogs survived likewise for longer periods, diffuse fibrosis all over the liver was also observed.

iii) The other organs

Thickening of the arterial wall, parenchymal atrophy were observed in the spleen. Macroscopically marked shrinkage of the greyish spleen was observed almost constantly in early period of the liver congestion.

Flattening, swelling of the tubulus and edema in the interstitial tissues of the kidney were observed in a few cases, but in many cases no specific changes were demonstrated microscopically as well as macroscopically. In the oesophagus, dilatation of the submucous vein was not observed in all cases.

IV. DISCUSSION

Obstruction of the inferior vena cava above hepatic level had attracted for years the attention of physicians because of its characteristic clinical symptoms and of its fatality. It was revealed by many clinical reports that irreversible or fatal changes, such as far advanced congestion cirrhosis of the liver or hepatoma presumably secondarily occurred

were often observed simultaneously when the characteristic superficial collateral circulations were dominant and thus diagnosis was established. Of course it is desirable to take caval venograph in order to reach the final diagnosis in early stage of the disease, while it is hardly expectable to carry out this examination routinely in suspected cases before the characteristic symptoms become dominant. Accordingly, as noted in our previous papers, this disease was very often confused with cirrhosis of the liver, BANTI's syndrom, and other conditions which cause portal hypertention with occasional edema of the legs. Hence, it seems desirable to find out a certain characteristic alterations to be observed even in early stages of this condition in some examinations more routinely performed.

Since the use of ^{198}Au colloid was recommended by SHEPPARD et al.[31] for the measurement of hepatic blood flow, this method has been used by many investigators[20)23)31)36)37)], and today, it became a routine hepatic function test in many clinics. But in recent days, IIO[12)], PLAYOUST[28)], and ABE[2)] reported that the removal efficiency of ^{198}Au colloid (supplied from radiochemical centre, Harwell) in the liver is much lower than those which were reported in early literatures. Hence the amount of hepatic blood flow measured in the present experiment is not able to evaluate as an absolute value. But it is significant as a relative value, because, as WATANABE[37)] insisted in his recent report, the removal efficiency itself is constant in various conditions, and the alteration in ^{198}Au colloid clearance is proportional to that of effective hepatic blood flow in liver sinusoid. The reduction rate of 28% in the estimated hepatic blood flow demonstrated in the present experiment is original data but is nothing characteristic in itself, because reduction rate in this degree is also not rarely observed in the other hepatic diseases.

Since FAUVERT[5)] noted the diagnostic significance of the hepatic clearance ratio, several investigators have tried to demonstrate the dissociation between two kinds of hepatic clearance measured by using two different materials, each of which was corresponding two different hepatic functions.

It seems somewhat strange that the BSP clearance remained nearly normal for a long period after the operation, notwithstanding the fact that BSP clearance is known as an indicator for function of the hepatic polygonal cells which are influenced to a certain degree by the alteration in hepatic blood flow. But as is well known, function of the hepatic polygonal cells have a good deal of reserve capacity, and have many different functions, therefore it seems rational to consider that BSP clearance is less influenced by a simple hemodynamic alteration in the liver than ^{198}Au colloid clearance which alter proportionally to the effective hepatic blood flow.

It is reported that clearance ratio K BSP/K ^{198}Au is invariable or only slightly increased in the clinical cases of cirrhosis of the liver or BANTI's disease, hence it seems to have some diagnostic significance that the marked increasing rate of 40% was observed in clearance ratio in constriction or obstruction of the inferior vena cava above hepatic level in the present experiment.

Regarding the observations in development of collateral circulation, little is added to the previous reports of the other authors[4)9)18)39)].

It is interesting that the special type of shrinkage of the liver was observed only in a few cases and not observed in the others in which the vessel was constricted in same

degree and survived for nearly the same periods. Further experiments should be required to clarify the cause of this point.

V. SUMMARY AND CONCLUSIONS

Experimental gradual constriction was succesfully produced in the thoratic inferior vena cava of dogs by means of modified NAKAMURA's method in order to survive the animals for a long period after the operation. The results revealed that this method is recommendable for this purpose.

Alterations in ^{198}Au colloid clearance, BSP clearance, and circulating blood volume were followed up throughout the course after the operation, and using the resulting data, estimated hepatic blood flow and clearance ratio were calculated.

1) ^{198}Au clearance reduced in early period when the constriction was first demonstrated in venograph, and remained in the lowered level over a long period of time, while circulating blood volume remained in nearly normal level or slightly increased. Therefore, the average rate of reduction in estimated hepatic blood flow was 28%.

2) The initial reduction was not observed in BSP clearance, hence the rate of increase in clearance ratio reached nearly 40% in the early period. This result is somewhat characteristic comparing with clearance ratios in the other hepatic disease.

3) In parallel with these pathophysiological measurements, development in collateral circulation was pursued by venograph. Two types of collateral circulation were observed there, namely the one was paravertebral type, and the other was parietal type.

4) The autopsy and pathohistological observation revealed the congestion of the liver in varying degree. In later periods, cirrhotic changes tended to be dominant, and a special type of shrinkage of the liver was observed, in which the cirrhotic changes were limited only in perilobar part.

No specific changes were observed in the other abdominal organs except the extreme phlebosclerosis in the abdominal inferior vena cava.

I would like to express my deep gratitude to Prof. Dr. CHUJI KIMURA for his cordial guidance throughout this experiment.

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PHOTO EXPLANATIONS

Photo. 1 Ascites accumlation and superficial collateral circulation developed following the constriction

Photo. 2 The thoracic inferior vena cava constricted by the granulation tissue developed inside the aluminium plate

Photo. 3 Shrinkage of the liver with entirely rounded edges : Note the extreme thickening of the liver capsule looking like "sugar coat"

Photo. 4 Autopsy : Note the congestion of the liver and dilated v. azygos

Photo. 5 Development of the collateral circulation : parietal type

Photo. 6 Development of the collateral circulation : paravertebral type

Photo. 7 The extreme thickening in the liver capsule

Photo. 8 The extreme thickening in the wall of hte inferior vena cava below its constricted portion : Note the partial thickening in the intima

Photo. 9 a) b) c) d) Congestion in varying degree in the liver ; atrophy and degeneration in hepatic parenchymal cells

Photo. 10 Cirrhotic changes in the liver : a) b) d)

c) Note the cirrhotic changes limited in perilobar part (downwards)

Photo. 1

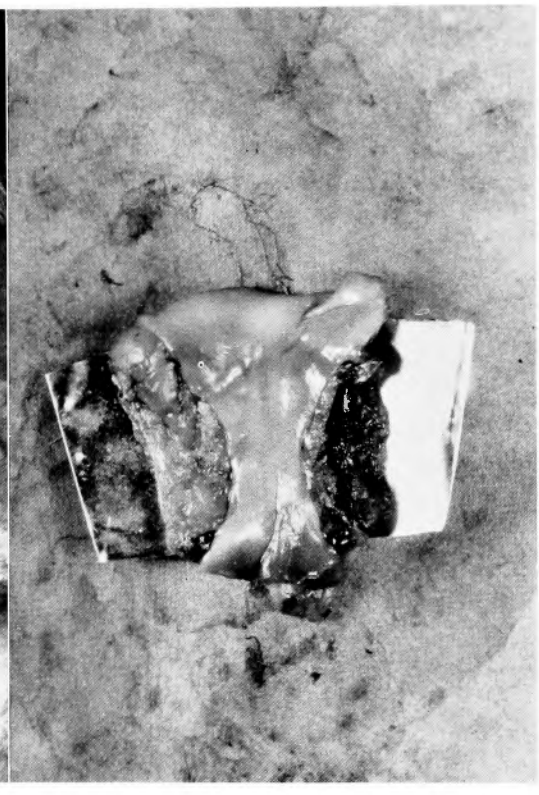


Photo. 2

Photo. 3

Photo. 4

Photo. 5

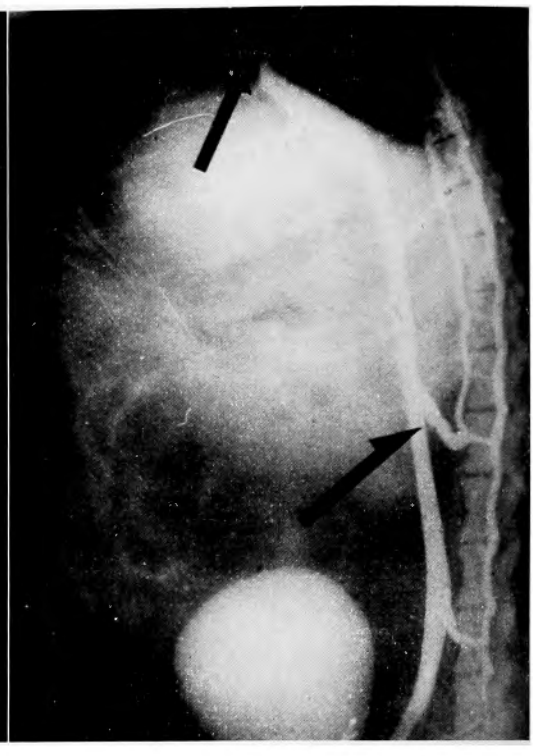
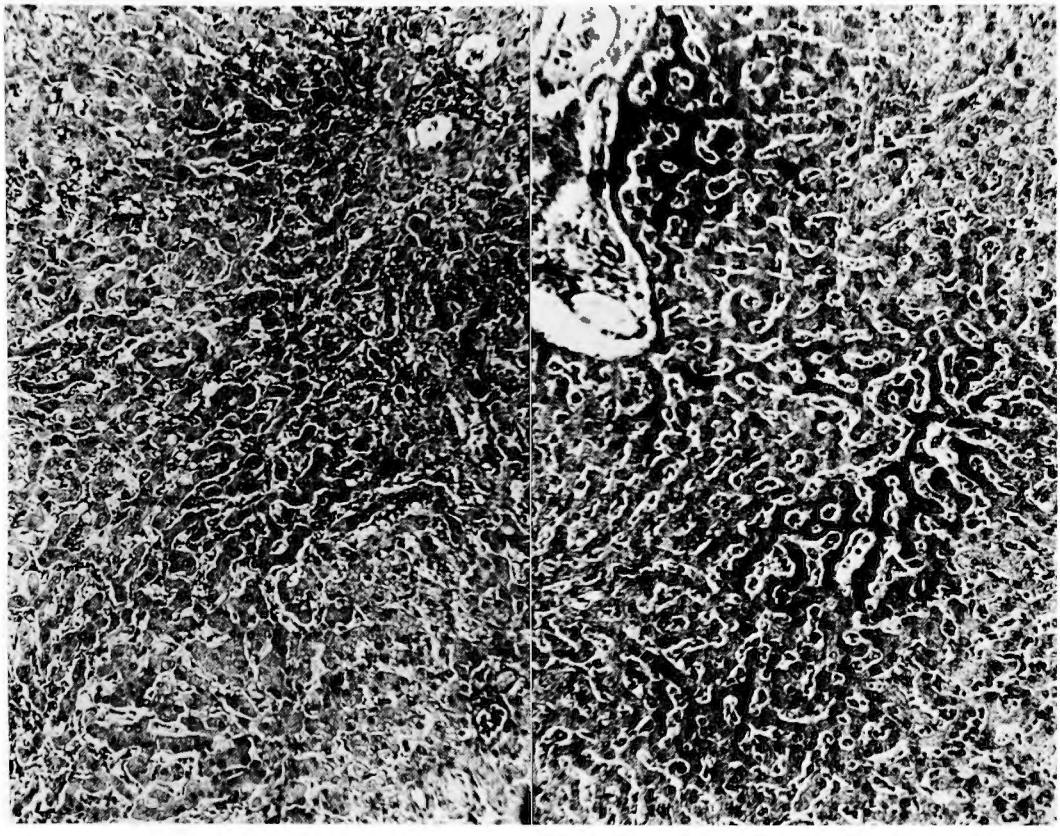


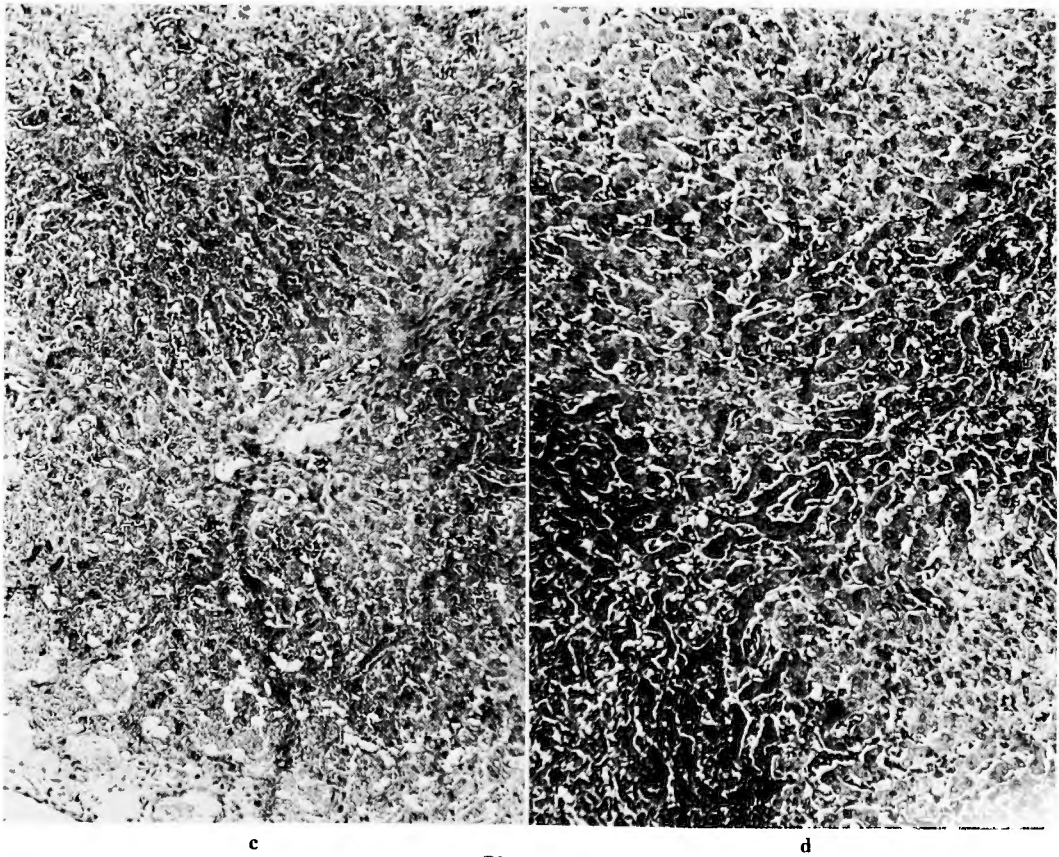
Photo. 6

Photo. 7

Photo. 8

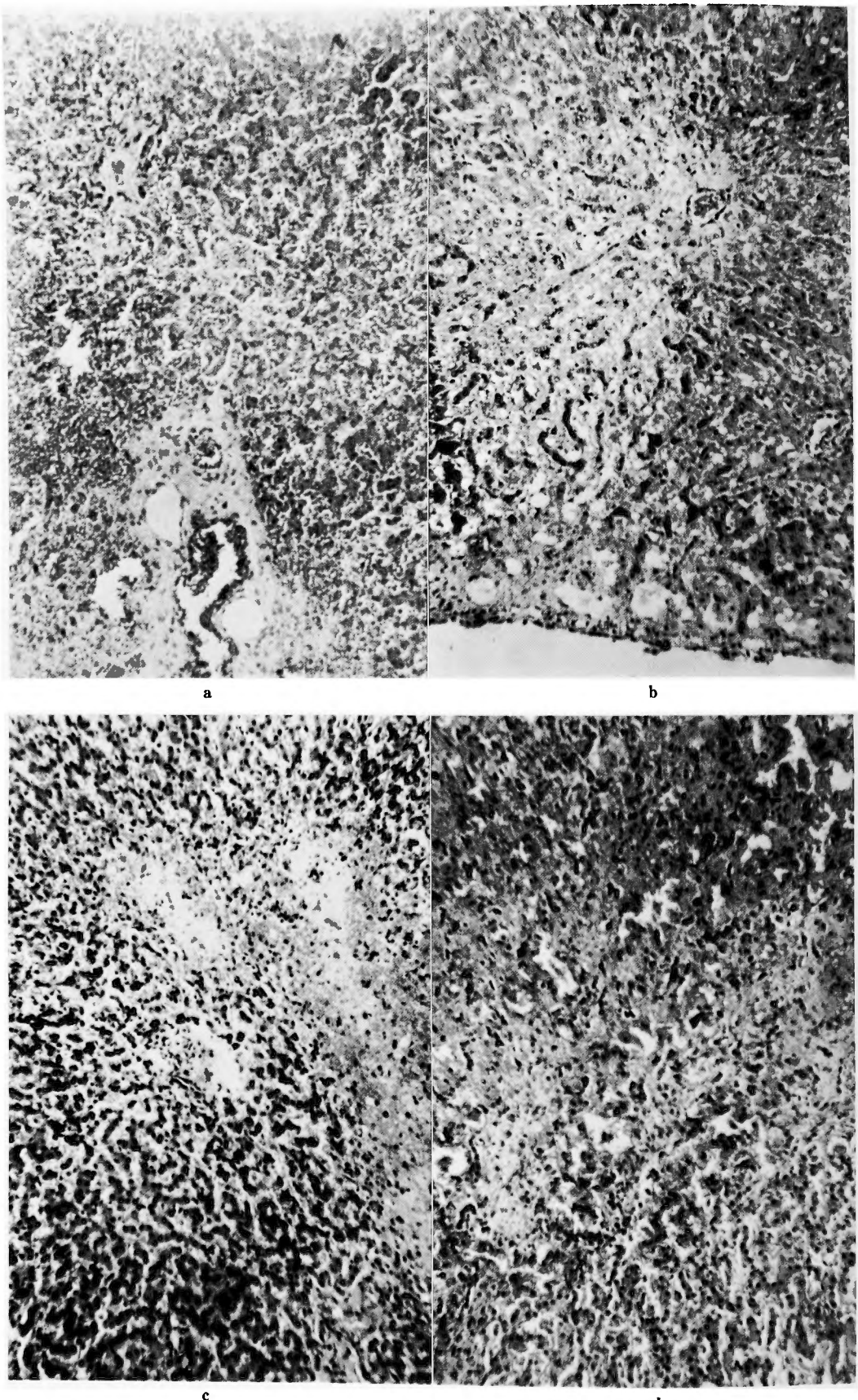


a b



c d

Photo. 9



a b

c d

Photo. 10

和文抄録

胸部下大静脈狭窄犬に関する実験的研究 特にその肝クレアランスの変化について

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肝静脈開口部より中枢側における下大静脈の狭窄や閉塞は，その高い致命率と特徴的な臨床症状により古来から医家の注意をひいて来た疾患であるが，その或種の症例は最近外科的治療の対象となつて来た．従来，本症は肝硬変やバンチ氏病と誤られる事が多く，その特徴的な表在性側副血行の発達によつて，容易に診断されうるような時期には，しばしば高度のうつ血性肝硬変などの致命的な病変を伴うことが知られている．以下の実験は，本症の経過について何らかの知見をうることを目標として犬を使用して実験的胸部下大静脈狭窄を作成し，特にその肝機能における変化を長期に亘つて追求したものである．動物を術後長期間生存させるためには，漸次に狭窄を行なうのが望ましいと考えて，肉芽腫促進物質 dicetyl phosphate を用いる中村氏法を胸部下大静脈に応用した．作成された漸次的胸部下大静脈狭犬のうち，完全閉塞の2例を含めて，狭窄が術前直径の1/2以上に進行し，かつ長期生存した例について，次の各項目における変化を最長2年に亘つて追求した．

1) 肝血行動態における変化をしらべるために，約3ヵ月ごとに放射性金コロイド ^{198}Au クレアランス及び循環血液量を測定し，これらより肝血流量を算出した．

2) 最近その診断的意義が注目されている肝クレアランス比，即ち肝実質細胞機能と肝星細胞機能の比の変化を追求するために，上記測定と同時に実質細胞機能を表す BSP クレアランスの測定を行ない，これと，星細胞機能をあらわす ^{198}Au クレアランスとの比を算出した．

3) 側副血行の発達を観察するために，約6ヵ月毎に大腿静脈よりカテーテルを挿入して2方向より静脈撮影を行なつた．

4) 約6ヵ月毎に一部の犬を薬殺して剖検し，その腹腔内臓器の組織標本を作成して観察した．得られた結果は次の通りである．

1) 正常犬における術前値の平均は，それぞれ ^{198}Au クレアランス係数 0.324min^{-1}，BSP クレアランス係数0.189min^{-1}，肝血流量は 39.12cc/min/kg であつた．

2) 肝血流量は腹水の発生が認められるようになると減少するが，その後は比較的一定している．術後平均減少率は28%であつた．

3) クレアランス比 $C_{BSP}/C_{^{198}Au}$ は術後平均約40%の増加率を示したが，更にすすんで組織学的に鬱血性肝硬変が認められる時期になると低下する傾向を示した．肝硬変やバンチ氏病の臨床例においては，クレアランス比がほぼ正常であることと比較して，興味ある結果であると思われる．

4) 側副血行の発達系路には，腰静脈，上行腰静脈，椎骨静脈，奇静脈等よりなる深部系と，浅，下腹壁静脈，内乳静脈等よりなる浅部系がみられるが，前者の方が早期に発達する傾向がある．

5) 初期には組織学的に肝小葉中心部より次第に小葉周辺部に波及してゆく鬱血像と肝実質細胞の萎縮・変性が認められ，より進んだ時期においては線維化の傾向が次第に著明となつて肝硬変に陥つてゆくのが観察された．一部の例では肉眼的に肝の高度の縮少と鈍縁化及び肝被膜の糖衣様肥厚が認められたが，この様な例では組織的に硬変が肝葉の周辺部にのみ限局され，中心部は正常の構造をのこしている特異な像がみられた．